Mary P. Edmonds (1922–2005)

When Mary P. Edmonds died of complications related to a heart attack on April 16, 2005, we lost a kind friend, gracious colleague, and mentor. But there is reason to celebrate the life of an inspired scientist whose seminal research virtually jump-started current RNA research in both 3′ end processing and splicing.

Mary was born in Racine, Wisconsin, 82 years ago, earned a B.A. at Milwaukee-Downer College in 1943, an M.A. at Wellesley College in 1945, and a Ph.D. at the University of Pennsylvania in 1951. In 1955, she began her long career in Pittsburgh as a research associate and remained in the research track for many years. She was named Associate Professor of Biochemistry in Arts and Sciences in 1971 and was promoted to Professor of Biological Sciences in 1976. She was named Professor Emeritus in 1992 but remained active in seminars and dissertation committees at Pitt and elsewhere until quite recently. Maybe you met her at your poster at an RNA meeting where she was a frequent participant. Mary loved poster sessions where she could interact with students and discuss their experiments at leisure.

As a biochemist, Mary characterized an enzyme that added A's to the 3′ ends of RNA and then showed in a PNAS paper in 1971[1] that eukaryotic mRNAs were made with these tails in vivo. Two other groups shared in that discovery by publishing back-to-back articles in the same journal. Mary subsequently showed that some viral RNAs also contained polyA even packaged in their virions. As a result of these papers, the field took off. This growth was based not only on the importance of the 3′-end-addition reaction but also on the ease with which the polyA tail itself provided a convenient hook to grab mRNAs out of the cell and study their dynamics. The enzyme Mary studied in a joint effort with Marv Wickens in 1990 was shown to be the nuclear polyA polymerase. In the years since 1971, the significance of the polyA tail and the vital function it serves in mRNA transport, stability, and translation has become clear. We now know that the amounts of the enzymes involved with the cleavage/polyadenylation reactions vary with a number of physiological parameters, thereby regulating not only the amount of pre-RNA processed into message but also the choice among polyA sites on complex transcripts, which themselves can influence stability and translation. The polyA tail is also a focus for binding by a number of factors that interact with the translational apparatus, modulating mRNA expression and decay. A woman whose tenacity to RNA research spanned over five decades made all of this possible.

Mary Edmonds' continued work on the chemical composition of polyA mRNA set the stage for the elucidation of the mechanism of nuclear pre-mRNA splicing. In the early

[1]Edmonds, Vaughan, and Nakazato, 1971. Polyadenylic acid sequences in the heterogeneous nuclear RNA and rapidly-labeled polyribosomal RNA of HeLa cells: possible evidence for a precursor relationship. *Proc. Natl. Acad. Sci.* **68:** 1336–1340.

1980s, her work with graduate student John Wallace demonstrated the presence of branched nucleotide structures in nuclear polyA mRNAs.[2] In these experiments, frighteningly large doses of ^{32}P-labeled inorganic phosphate (by today's standards) were used for metabolic labeling of HeLa cell RNAs, which were then purified from nuclear or cytoplasmic cell fractions using oligodT columns. These purified RNAs were then reduced to their basic nucleotide building blocks by exhaustive digestion with ribonuclease T2, which normally cleaves on the 3′ side of each nucleotide (A, C, G, and U) in single-stranded RNA. The reaction products, which were expected to contain cap dinucleotides and mononucleotides with 5′-hydroxyl and 3′-monophosphate structures, were separated by DEAE-cellulose chromatography. Surprisingly, in addition to the expected cap dinucleotide and mononucleotide products, more highly charged ribonuclease-T2-resistant products were also detected. These resistant products proved to be trinucleotides that contained both 2′-5′ and 3′-5′ phosphodiester bonds attached to the same ribose ring. The Edmonds lab carefully confirmed these results using chemical cleavage methods and additional ribonucleases to elucidate the composition of these trinucleotides. They also noted a key feature of the biology of branched trinucleotides—they were enriched in nuclear, but not cytoplasmic, mRNA. These observations led Mary Edmonds to propose that branched trinucleotides might be integral components of the intermediates involved in pre-mRNA splicing. The timing of the Wallace and Edmonds 1981 publication could not have been better. In the subsequent months, papers from the Maniatis and Sharp labs described the lariat intron product and intermediate of the nuclear pre-mRNA splicing reaction, which soon thereafter were shown to have a branched adenosine trinucleotide with 2′-5′ and 3′-5′ linkages.

For her major contributions to RNA processing, Mary Edmonds was elected to the National Academy of Sciences in 1991 and received several honorary doctorates from various colleges. We will remember her quiet grace, keen scientific insight, and unwavering determination.

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[2]Wallace and Edmonds, 1981. Polyadenylated nuclear RNA contains branches. *Proc. Natl. Acad. Sci.* **80:** 950–954.